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A Study to Characterize Regimens of Basal Insulin Intensified With Either Symlin® or Rapid Acting Insulin in Patients With Type 2 Diabetes

This study has been completed.

 Study NCT00467649 Information provided by Amylin Pharmaceuticals, Inc.
 First Received: April 27, 2007 Last Updated: April 10, 2009 [History of Changes](#)

Study Type:	Interventional
Study Design:	Randomized, Open Label, Active Control, Parallel Assignment
Condition:	Type 2 Diabetes Mellitus
Interventions:	Drug: pramlintide acetate Drug: rapid acting insulin (Humalog® [insulin lispro], Novolog® [insulin aspart], or Apidra® [insulin glulisine]) Drug: basal insulin (Lantus® [insulin glargine], or Levemir® [insulin detemir])

Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study
Group C (P2 SYMLIN)	Patients from Group A, who achieved HbA1c goal at Week 24, continued Phase 1 treatment during Phase 2
Group D (P2 SYMLIN+RA)	Patients from Group A, who did not achieve HbA1c goal at Week 24, continued phase 1 treatment and initiated RA insulin during Phase 2
Group E (P2 RA Insulin)	Patients from Group B, who achieved HbA1c goal at Week 24, continued Phase 1 treatment during Phase 2
Group F (P2 RA Insulin + SYMLIN)	Patients from Group B, who did not achieve HbA1c goal at Week 24, continued phase 1 treatment and initiated SYMLIN during Phase 2

Participant Flow for 2 periods

Period: Phase 1 (Intent-to-Treat Population)

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)	Group C (P2 SYMLIN)	Group D (P2 SYMLIN+RA)	Group E (P2 RA Insulin)	Group F (P2 RA Insulin + SYMLIN)
STARTED	56	56	0	0	0	0
COMPLETED	48	50	0	0	0	0
NOT COMPLETED	8	6	0	0	0	0
Adverse Event	2	0	0	0	0	0
Investigator Decision	1	0	0	0	0	0
Lost to Follow-up	2	4	0	0	0	0
Withdrawal of Consent	3	2	0	0	0	0

Period: Phase 2 (Intent-to-Treat Population)

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)	Group C (P2 SYMLIN)	Group D (P2 SYMLIN+RA)	Group E (P2 RA Insulin)	Group F (P2 RA Insulin + SYMLIN)
STARTED	0	0	17	31	14	36
COMPLETED	0	0	17	29	14	35
NOT COMPLETED	0	0	0	2	0	1
Lost to Follow-up	0	0	0	1	0	0
Protocol Violation	0	0	0	1	0	0
Withdrawal of Consent	0	0	0	0	0	1

► Baseline Characteristics

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Baseline Measures

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)	Total
Number of Participants (units: participants)	56	56	112
Age (units: participants)			
<=18 years	0	0	0
Between 18 and 65 years	46	49	95
>=65 years	10	7	17
Age (units: years) Mean ± Standard Deviation	55.0 ± 11.35	53.6 ± 9.70	54.3 ± 10.53
Gender (units: participants)			
Female	22	19	41
Male	34	37	71
Region of Enrollment (units: participants)			
United States	56	56	112
Fasting Plasma Glucose (units: mg/dL) Mean ± Standard Deviation	155.1 ± 39.60	164.3 ± 49.61	159.7 ± 44.92
Fasting Serum Lipids (units: mg/dL) Mean ± Standard Deviation			
Total Cholesterol	167.53 ± 47.054	169.86 ± 49.121	168.70 ± 47.903
HDL	44.71 ± 11.893	41.77 ± 9.468	43.23 ± 10.790
LDL	89.15 ± 38.386	90.41 ± 34.114	89.78 ± 36.133
Triglycerides	174.13 ± 108.257	193.59 ± 159.508	183.95 ± 136.273
HbA1c (units: %) Mean ± Standard Deviation	8.19 ± 0.840	8.25 ± 0.816	8.22 ± 0.825
Waist Circumference (units: cm) Mean ± Standard Deviation	116.31 ± 15.427	117.15 ± 13.198	116.73 ± 14.297
Weight (units: kg) Mean ± Standard Deviation	107.87 ± 21.893	103.46 ± 17.908	105.67 ± 20.032

► Outcome Measures

 Hide results for all outcome measures

1. Primary Outcome Measure: The Proportion of Patients Achieving HbA1c <=7% at Week 24 With no Gain in Body Weight From Baseline and no Incidence of Severe Hypoglycemia

Measure Type	Primary
Measure Title	The Proportion of Patients Achieving HbA1c <=7% at Week 24 With no Gain in Body Weight From Baseline and no Incidence of Severe Hypoglycemia
Measure Description	Comprehensive treatment endpoint assessing the achievement of glycemic control without weight gain and severe hypoglycemia. The patient must achieve each component of the endpoint to count towards the final percentage.
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 1 Intent-to-Treat LOCF. LOCF: If a treated patient has missing result value at week 24, then last observed value before week 24 and after baseline is carried forward to impute the week 24 value.

Reporting Groups

	Description

Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin; variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	56	56
The Proportion of Patients Achieving HbA1c <=7% at Week 24 With no Gain in Body Weight From Baseline and no Incidence of Severe Hypoglycemia [units: %]	30.4	10.0

Statistical Analysis 1 for The Proportion of Patients Achieving HbA1c <=7% at Week 24 With no Gain in Body Weight From Baseline and no Incidence of Severe Hypoglycemia

Groups ^[1]	All groups
Method ^[2]	Fisher Exact
P Value ^[3]	0.0180

[1] Additional details about the analysis, such as null hypothesis and power calculation:

No text entered.

[2] Other relevant information, such as adjustments or degrees of freedom:

No text entered.

[3] Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

No text entered.

2. Secondary Outcome Measure: Proportion of Patients Achieving HbA1c <=7% at Week 24

Measure Type	Secondary
Measure Title	Proportion of Patients Achieving HbA1c <=7% at Week 24
Measure Description	This is a component of the primary endpoint
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Phase 1 Intent-to-Treat

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal Insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin; variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	56	56
Proportion of Patients Achieving HbA1c <=7% at Week 24 [units: %]	44.6	55.4

No statistical analysis provided for Proportion of Patients Achieving HbA1c <=7% at Week 24

3. Secondary Outcome Measure: Proportion of Patients With no Weight Gain at Week 24

Measure Type	Secondary
Measure Title	Proportion of Patients With no Weight Gain at Week 24
Measure Description	This is a component of the primary endpoint
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Phase 1 Intent-to-Treat

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	56	56
Proportion of Patients With no Weight Gain at Week 24 [units: %]	46.4	14.3

No statistical analysis provided for Proportion of Patients With no Weight Gain at Week 24

4. Secondary Outcome Measure: Proportion of Patients With a Severe Hypoglycemia Adverse Event

Measure Type	Secondary
Measure Title	Proportion of Patients With a Severe Hypoglycemia Adverse Event
Measure Description	This is a component of the primary endpoint
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Phase 1 Intent-to-Treat

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	56	56
Proportion of Patients With a Severe Hypoglycemia Adverse Event [units: %]	0.0	0.0

No statistical analysis provided for Proportion of Patients With a Severe Hypoglycemia Adverse Event

5. Secondary Outcome Measure: Change in HbA1c From Baseline at Week 24

Measure Type	Secondary
Measure Title	Change in HbA1c From Baseline at Week 24
Measure Description	No text entered.
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Phase 1 Intent-to-Treat LOCF. LOCF: If a treated patient has missing result value at week 24, then last observed value before week 24 and after baseline is carried forward to impute the week 24 value.

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	56	56
Change in HbA1c From Baseline at Week 24 [units: %] Least Squares Mean \pm Standard Error	-1.11 \pm 0.17	-1.27 \pm 0.17

No statistical analysis provided for Change in HbA1c From Baseline at Week 24

6. Secondary Outcome Measure: Change in Body Weight From Baseline at Week 24

Measure Type	Secondary
Measure Title	Change in Body Weight From Baseline at Week 24
Measure Description	No text entered.
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 1 Intent-to-Treat LOCF. LOCF: If a treated patient has missing result value at week 24, then last observed value before week 24 and after baseline is carried forward to impute the week 24 value.

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	56	56
Change in Body Weight From Baseline at Week 24 [units: kg] Least Squares Mean \pm Standard Error	0.02 \pm 0.68	4.65 \pm 0.68

No statistical analysis provided for Change in Body Weight From Baseline at Week 24

7. Secondary Outcome Measure: Change in Waist Circumference From Baseline

Measure Type	Secondary
Measure Title	Change in Waist Circumference From Baseline
Measure Description	No text entered.
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 1 Intent-to-Treat LOCF. LOCF: If a treated patient has missing result value at week 24, then last observed value before week 24 and after baseline is carried forward to impute the week 24 value.

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed [units: participants]	53	56
Change in Waist Circumference From Baseline [units: cm] Least Squares Mean \pm Standard Error Change at Week 24	-0.63 \pm 0.87	2.17 \pm 0.86

No statistical analysis provided for Change in Waist Circumference From Baseline

8. Secondary Outcome Measure: Change in Fasting Plasma Glucose From Baseline

Measure Type	Secondary
Measure Title	Change in Fasting Plasma Glucose From Baseline
Measure Description	No text entered.
Time Frame	24 Weeks

Safety Issue	No
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Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 1 Intent-to-Treat

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed (units: participants)	45	50
Change in Fasting Plasma Glucose From Baseline (units: mg/dL) Mean \pm Standard Error		
Change at Week 24	-29.0 \pm 7.32	-37.8 \pm 7.69

No statistical analysis provided for Change in Fasting Plasma Glucose From Baseline

9. Secondary Outcome Measure: Fasting Serum Lipids Change From Baseline at Week 24

Measure Type	Secondary
Measure Title	Fasting Serum Lipids Change From Baseline at Week 24
Measure Description	No text entered.
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 1 Intent-to-Treat

Reporting Groups

	Description
Group A (P1 SYMLIN)	SYMLIN treatment (120 mcg prior to major meals) was initiated on Day 1. Basal insulin was titrated throughout the study
Group B (P1 RA Insulin)	Rapid acting insulin (RA Insulin: variable dosing, titrated to optimize postprandial glucose control) was initiated at Week 4. Basal insulin was titrated throughout the study

Measured Values

	Group A (P1 SYMLIN)	Group B (P1 RA Insulin)
Number of Participants Analyzed (units: participants)	47	49
Fasting Serum Lipids Change From Baseline at Week 24 (units: mg/dL) Mean \pm Standard Error		
Total Cholesterol	-1.81 \pm 5.826	5.27 \pm 4.649
HDL	1.11 \pm 1.190	1.65 \pm 1.075
LDL	2.36 \pm 4.456	9.12 \pm 3.865
Triglycerides	-28.96 \pm 12.442	-31.98 \pm 13.883

No statistical analysis provided for Fasting Serum Lipids Change From Baseline at Week 24

10. Secondary Outcome Measure: Phase 2: Change in HbA1c at Week 36

Measure Type	Secondary
Measure Title	Phase 2: Change in HbA1c at Week 36
Measure Description	No text entered.
Time Frame	36 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 2 Intent-to-Treat

Reporting Groups

	Description
Group C (P2 SYMLIN)	Patients from Group A, who achieved HbA1c goal at Week 24, continued Phase 1 treatment during Phase 2
Group D (P2 SYMLIN+RA)	Patients from Group A, who did not achieve HbA1c goal at Week 24, continued phase 1 treatment and initiated RA insulin during Phase 2
Group E (P2 RA Insulin)	Patients from Group B, who achieved HbA1c goal at Week 24, continued Phase 1 treatment during Phase 2
Group F (P2 RA Insulin + SYMLIN)	Patients from Group B, who did not achieve HbA1c goal at Week 24, continued phase 1 treatment and initiated SYMLIN during Phase 2

Measured Values

	Group C (P2 SYMLIN)	Group D (P2 SYMLIN+RA)	Group E (P2 RA Insulin)	Group F (P2 RA Insulin + SYMLIN)
Number of Participants Analyzed [units: participants]	17	30	14	36
Phase 2: Change in HbA1c at Week 36 [units: %] Mean ± Standard Error				
Change From Baseline	-1.96 ± 0.238	-0.68 ± 0.174	-1.49 ± 0.189	-0.99 ± 0.157
Change From Week 24	0.14 ± 0.062	-0.23 ± 0.123	0.22 ± 0.097	0.07 ± 0.113

No statistical analysis provided for Phase 2: Change in HbA1c at Week 36

11. Secondary Outcome Measure: Phase 2: Change in Body Weight at Week 36

Measure Type	Secondary
Measure Title	Phase 2: Change in Body Weight at Week 36
Measure Description	No text entered.
Time Frame	36 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Phase 2 Intent-to-Treat

Reporting Groups

	Description
Group C (P2 SYMLIN)	Patients from Group A, who achieved HbA1c goal at Week 24, continued Phase 1 treatment during Phase 2
Group D (P2 SYMLIN+RA)	Patients from Group A, who did not achieve HbA1c goal at Week 24, continued phase 1 treatment and initiated RA insulin during Phase 2
Group E (P2 RA Insulin)	Patients from Group B, who achieved HbA1c goal at Week 24, continued Phase 1 treatment during Phase 2
Group F (P2 RA Insulin + SYMLIN)	Patients from Group B, who did not achieve HbA1c goal at Week 24, continued phase 1 treatment and initiated SYMLIN during Phase 2

Measured Values

	Group C (P2 SYMLIN)	Group D (P2 SYMLIN+RA)	Group E (P2 RA Insulin)	Group F (P2 RA Insulin + SYMLIN)
Number of Participants Analyzed [units: participants]	17	30	14	36
Phase 2: Change in Body Weight at Week 36 [units: kg] Mean ± Standard Error				
Change From Baseline	-0.80 ± 2.096	1.34 ± 0.933	3.90 ± 1.488	4.51 ± 0.761
Change From Week 24	0.69 ± 0.854	0.50 ± 0.303	0.44 ± 0.518	-0.86 ± 0.353

No statistical analysis provided for Phase 2: Change in Body Weight at Week 36

► Reported Adverse Events

No Adverse Events Entered.

► More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

- ☒ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.
- ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.
- ☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

Results Point of Contact:

Name/Title: Chief Medical Officer
 Organization: Amylin Pharmaceuticals Inc
 e-mail: clinicaltrials@amylin.com

No publications provided

Responsible Party: Amylin Pharmaceuticals (Lisa Porter, MD, Study Director)
 Study ID Numbers: ACA401
 Study First Received: April 27, 2007
 Results First Received: April 10, 2009
 Last Updated: April 10, 2009
 ClinicalTrials.gov Identifier: NCT00467649 [History of Changes](#)
 Health Authority: United States: Institutional Review Board

Contact/Help Desk
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